Antibodies to CD52g, a Secreted Sperm coating Antigen, Agglutinate Seminal Leukocytes and Prevent their Infiltration into Vaginal Epithelium

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Abstract

Introduction:
Our program is studying the topical use of monoclonal antibodies (mAbs) for contraception and HIV prevention. mAbs directed against CD52g, an antigen secreted into the male genital tract and inserted into sperm membranes, potently agglutinate sperm and are being developed for contraceptive use. We are also seeking strategies to prevent cell-associated HIV transmission mediated by HIV-infected seminal white blood cells (sWBC). In this study, we investigated whether CD52g also attaches to sWBC, and whether anti-CD52g mAbs agglutinate these cells and/or inhibit their interaction with the vaginal epithelium.

Methods and Materials:
Dylight 633-conjugated MSH8, a mouse anti-CD52g mAb (gift of J. Herr), was used in Flow cytometry experiments to detect CD52g on sWBC and passive insertion of seminal plasma CD52g into the plasma membrane of monocyte-derived macrophages (MDMs). HC4, a human mAb expressed in Nicotiana (Mapp Biopharmaceuticals), was used in two functional assays: 1) agglutination of sWBC, assessed by counting the percentage of CMFDA-labelled WBC associated with sperm agglutinates in mAb-treated seminal fluid; and 2) cell attachment and infiltration assays, modeled with CD52g-coated CMFDA-labelled WBCs and EpiVaginal™ tissue (MatTek Corp), and assessed by confocal microscopy. Infiltrated cells were counted using ImageJ software. ANOVA with post-hoc Fisher’s PLSD comparison was used for statistical analysis.

Results:
MSH8 bound to a majority of sWBCs and also to seminal plasma-treated peripheral blood mononuclear cells (PBMCs). HC4 trapped WBCs in sperm agglutinates. The antibody also significantly inhibited the attachment and infiltration of CD52g-coated WBCs into the vaginal epithelium. Control mAbs had no effect in these assays.

Conclusions

• Anti-CD52g was detected on cell membranes of seminal leukocytes from a variety of semen donor types including normozoospermic and vasectomized.
• HC4 plantibody, a potent sperm agglutinating antibody, trapped seminal WBCs with the spermatozoon.
• HC4 plantibody significantly blocked adhesion and infiltration of MDMs into EpiVaginal tissue.
• Topical vaginal application of antibodies to CD52g could serve a dual purpose use: contraception and inhibition of cell-associated HIV transmission.

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